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Docket No. G-085US04CON
Serial No. 09/818,260In the Claims

1. (Currently Amended) A method of determining the statistical significance of a difference between haplotype frequency profiles of ~~a least at least~~ two groups of individuals comprising:

- a) obtaining ~~and assigning~~ haplotypes ~~to for~~ all individuals in one of said at least two groups of individuals by genotyping the same chromosomal segment;
- b) obtaining ~~and assigning~~ haplotypes ~~to for~~ all individuals in another of said at least two groups of individuals by genotyping the same chromosomal segment;
- c) identifying the haplotypes of all individuals in each of said at least two groups with using a binary code to generate a binary mask array;
- d) analyzing the haplotypes of said at least two groups of individuals comprising the steps of:

determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the difference of said sum and said combined likelihood; and

determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes.

2-3. (Canceled)

4. (Currently Amended) A system for determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals, comprising:

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~~first instructions that assign a binary code to the haplotype of each individual for identifying the haplotypes of all individuals in each of said at least two groups of individuals using a binary code to generate a binary mask array;~~

~~second instructions for determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;~~

~~third instructions for determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;~~

~~fourth instructions for determining the difference of said sum and said combined likelihood;~~
~~and~~

~~fifth instructions for determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes;~~

~~wherein said system comprises one or more electronically connected computers executing software obtained by linking modules of programs and stored on programmed storage devices a programmed storage device comprising at least one module or one or more computer.~~

5-6. (Canceled)

7. (Currently Amended) A programmed storage device comprising instructions that when executed perform a method comprising:

~~assigning a binary code to the haplotype of each individual of said at least two groups of individuals;~~

~~determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals by comprising comparing the final likelihood that all groups of individuals come from the same distribution of haplotypes with the sum of the final likelihoods for each group separately; and~~

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determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes.

8-39. (Canceled)

40. (Currently Amended) A method of determining the statistical significance of a difference between haplotype frequency profiles of at least at least two groups of individuals comprising:

- a) obtaining and assigning haplotypes to all individuals in one of said at least two groups of individuals by genotyping the same chromosomal segment;
- b) obtaining and assigning haplotypes to all individuals in another of said at least two groups of individuals by genotyping the same chromosomal segment;
- c) identifying the haplotypes of all individuals in each of said at least two groups with using a binary code to generate a binary mask array;
- d) calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype; and
- d) e) analyzing the haplotypes of said at least two groups of individuals to determine the statistical significance of a difference between haplotype frequency profiles of said at least two groups of individuals comprising the steps of:

determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

determining the difference of said sum and said combined likelihood; and

determining the statistical significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes; and

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~~e) -----further comprising the step of calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype.~~

41. (Currently Amended) A method of determining the statistical significance of a difference between haplotype frequency profiles of a least at least two groups of individuals comprising:

a) ~~obtaining and assigning haplotypes to all individuals in one of said at least two groups of individuals by genotyping the same chromosomal segment;~~

b) ~~obtaining and assigning haplotypes to all individuals in another of said at least two groups of individuals by genotyping the same chromosomal segment;~~

c) ~~identifying the haplotypes of all individuals in each of said at least two groups with using a binary code to generate a binary mask array;~~

~~d) -----assessing the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype; and~~

~~d)e) analyzing the haplotypes of said at least two groups of individuals to determine the statistical significance of a difference between haplotype frequency profiles of said at least two groups of individuals comprising the steps of:~~

~~determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;~~

~~determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;~~

~~determining the difference of said sum and said combined likelihood; and~~

~~determining the statistical significance of the difference of said sum and said combined likelihood by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes; and~~

~~e) -----further comprising assessing the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype.~~

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42-45. (Canceled)

46. (Currently Amended) A system for determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals, comprising:

~~first instructions that assign a binary code to the haplotype of each individual for identifying the haplotypes of all individuals in each of said at least two groups of individuals using a binary code to generate a binary mask array;~~

~~second instructions for determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;~~

~~third instructions for determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;~~

~~fourth instructions for determining the difference of said sum and said combined likelihood;~~
and

~~fifth instructions for calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype-determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes; and~~

~~sixth instructions for determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes in order to determine the statistical significance of a difference between haplotype frequency profiles of said at least two groups of individuals calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype;~~

~~wherein said system comprises one or more electronically connected computers executing software obtained by linking modules of programs and stored on programmed storage devices a programmed storage device comprising at least one module or one or more computer.~~

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47. (Currently Amended) A system for determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals, comprising:

first instructions that assign a binary code to the haplotype of each individual for identifying the haplotypes of all individuals in each of said at least two groups of individuals using a binary code to generate a binary mask array;

second instructions for determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;

third instructions for determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes associated to a binary code;

fourth instructions for determining the difference of said sum and said combined likelihood; and

fifth instructions for calculating the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype; determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes; and

sixth instructions for determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes in order to determine the statistical significance of a difference between haplotype frequency profiles of said at least two groups of individuals; calculating the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype;

wherein said system comprises one or more electronically connected computers executing software obtained by linking modules of programs and stored on programmed storage devices; a programmed storage device comprising at least one module or one or more computer.

48. (Currently Amended) A programmed storage device comprising instructions that when executed perform a method comprising:

~~----- assigning a binary code to the haplotype of each individual of said at least two groups of individuals;~~

determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals by comprising comparing the final likelihood that all groups of individuals come from the same distribution of haplotypes with the sum of the final likelihoods for each group separately;

determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes; and

calculating the statistical significance of individual haplotypes using an odds ratio or a P-excess value in order to provide measures of association between groups for a particular haplotype.

49. (Currently Amended) A programmed storage device comprising instructions that when executed perform a method comprising:

~~----- assigning a binary code to the haplotype of each individual of said at least two groups of individuals;~~

determining the statistical significance of the difference between haplotype frequency profiles of at least two groups of individuals by comprising comparing the final likelihood that all groups of individuals come from the same distribution of haplotypes with the sum of the final likelihoods for each group separately;

determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes; and

calculating all possible single-haplotype chi-square tests in order to provide measures of association between groups for a particular haplotype.

50. (Currently Amended) A method of determining the statistical significance of a difference between haplotype frequency profiles of a least at least two groups of individuals comprising:

a) ~~obtaining and assigning haplotypes to all individuals in one of said at least two groups of individuals and coding said haplotypes with binary mask arrays by genotyping the same chromosomal segment;~~

b) ~~obtaining and assigning haplotypes to all individuals in another of said at least two groups of individuals and coding said haplotypes with binary mask arrays by genotyping the same chromosomal segment;~~

c) ~~identifying the haplotypes of all individuals in each of said at least two groups using a binary code to generate a binary mask array;~~

d) using said binary mask array for analyzing the haplotypes of said at least two groups of individuals comprising the steps of:

1) determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes;

2) determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes;

3) determining the difference of said sum and said combined likelihood; and

4) determining the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes.